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PATENT
Docket No. P-4423

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| APPLICANT(S): | D. J. Wright, M. A. Milla, J. G. Nadeau and G. T. Walker | | |
| SERIAL NO. | 09/335,218 | ART UNIT: | 1655 |
| FILING DATE: | June 17, 1999 | EXAMINER: | B. Forman |
| TITLE: | Methods and Oligonucleotides for Detecting Nucleic Acid Sequence Variations | | |

Assistant Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231
On: February 2, 2001
By: Donna M. Baumann
Donna M Baumann 2-2-01
(signature) (date)

**SUBMISSION UNDER 37 CFR §1.114**

This submission is filed in connection with the accompanying Request for Continued Examination of the subject patent application. An Office Action finally rejecting this application was mailed September 20, 2000. Applicants request withdrawal of the finality of that Office Action and entry and consideration of this submission. Please extend the time period for response by two months to February 20, 2001.

*IN THE CLAIMS*

Please amend the claims as follows:

55. (Amended) A method for detecting a single nucleotide polymorphism in a target sequence comprising:

a) hybridizing to the target sequence a detector primer comprising a diagnostic nucleotide for the single nucleotide polymorphism which is a 3' terminal nucleotide of the detector primer or about one to four nucleotides from the 3' terminal nucleotide;

*b)* in a primer extension reaction, displacing the detector primer by extension of a second primer hybridized to the target sequence upstream of the detector primer, and;

*c)* detecting the presence or absence of theh single nucleotide polymorphism based on an efficiency of detector primer extension.

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CX

*REMARKS*

The foregoing amendments are supported by the specification as filed and therefore do not introduce new matter. The position of the diagnostic nucleotide is recited in originally-filed Claim 1 and throughout the specification. Entry of the amendments is requested.

35 USC §102(e)

Claims 1-5, 14-18 and 24 are rejected as allegedly anticipated by Schram et al. partially on the basis that Schram et al. allegedly disclose a detector primer with a diagnostic nucleotide at the 3' terminus. Enclosed is the Declaration of James G. Nadeau rebutting this assertion. Dr. Nadeau establishes that the "diagnostic" nucleotide of Schram et al. is neither at the 3' terminus nor within about 1-4 nucleotides of the 3' terminus, as claimed. These claims are therefore not anticipated and withdrawal of the rejection is requested.

35 USC §103(a)

Dependent Claims 6-13, 19-21, 22 and 23, 1-22 and 24, and 22 and 23 are rejected as allegedly obvious over either Schram et al or Vary et al in view of several secondary references. In the enclosed Declaration, Dr. Nadeau addresses the teachings of the two primary references. He explains that although Schram et al. were able to distinguish the single nucleotide polymorphism using multiple primers containing diagnostic nucleotides in strand displacement detection reactions, they were not able to distinguish such SNP's when only a single detector primer containing a diagnostic nucleotide at the -12 position was employed. Schram et al. do not suggest any solution to this problem. However, Applicants have discovered that by moving the mismatch to the claimed positions this failure can be overcome and only a single detector primer is needed to distinguish the SNP. As Dr. Nadeau states, this discovery was unexpected and could not be deduced from the cited references. With respect to Vary et al., Dr. Nadeau declares that there is no suggestion in the cited prior art that the 3' terminal mismatch of Vary et al. would successfully solve the problem encountered by Schram et al. if applied to a strand displacing detection reaction. Further, there is no suggestion in the cited prior art to place the diagnostic nucleotide at about -1 to -4 of the primer for use in a strand displacing reaction.

Therefore the claimed method as set forth in the independent claims (Claim 1 and Claim 55) is neither anticipated or rendered *prima facie* obvious by the cited references. For this reason the rejections of dependent Claims 6-13, 19-21, 22 and 23, 1-22 and 24, and 22 and 23 under 35 USC 103(a)

relying on Schram et al. and Vary et al. as the primary reference is improper and should be withdrawn. For the reasons stated above, the rejection of new Claims 55-62 under §103(a) should also be withdrawn.

Double Patenting

Claims 1-8, 11, 12, 15-18 and 24 are rejected for obviousness type double-patenting over Claims 3, 7, 10 and 13 of Schram et al. Claims 1-8, 11-18 and 24 are similarly rejected over Claims 3, 7, 10 & 13 of Schram et al. The claims of Schram et al. recite SEQ ID NO:1 and either SEQ ID NO:2 or SEQ ID NO:3. None of these sequences have the mismatch in the recited position. Applicants have established that Schram et al. failed to successfully distinguish single nucleotide polymorphisms using one of these sequences and that it would not be obvious to move the mismatch to the presently claimed positions to overcome this failure problem. The Examiner's reference to Col. 5, Lns. 17-34 as showing placement of the diagnostic nucleotide at the 3' terminus is incorrect. That disclosure refers only to the position of the target binding sequence of the primer, not to the placement of the diagnostic nucleotide. As shown in the accompanying Declaration, the diagnostic nucleotides of the reference are not in the positions presently claimed. The claims of Schram et al. therefore do not render obvious the claimed invention and all obviousness type double-patenting rejections should be withdrawn.

*CONCLUSION*

In view of the foregoing amendments and remarks, Applicants respectfully submit that the present application is in condition for allowance. An action passing this case to issue is requested. If the Examiner is of the opinion that a telephone interview would be helpful to resolve any outstanding issues in this case, he/she is invited to call the undersigned at the number shown below.

Respectfully submitted,

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